

## Gouty Panniculitis also Involving the Bone Marrow

Chang-Min Choi<sup>1</sup>, Bark-Lynn Lew<sup>1\*</sup>, Sang-Ho Lee<sup>2</sup> and Woo-Young Sim<sup>1</sup>

Departments of <sup>1</sup>Dermatology and <sup>2</sup>Nephrology, College of Medicine, Kyung Hee University Hospital at Gangdong, #1 Sang-II Dong, Gang-Dong Ku, Seoul, 134-727, Korea. \*E-mail: bellotte@hanmail.net

Accepted May 1, 2012; Epub ahead of print Nov 29, 2012

Gout is a clinical syndrome presenting with recurrent, painful arthritis caused by deposition of monosodium urate. Urate crystal deposits are usually detected in the synovial membranes, joint capsules, articular cartilage, and periarticular tissue, and, rarely, in extra-articular areas (1). Gouty panniculitis is characterized by subcutaneous depositions of urate crystals with lobular panniculitis. We report here a case of this rare variant of gout, in a 47-year-old man who also showed characteristic depositions of crystals in the bone marrow.

### CASE REPORT

A 47-year-old man presented with skin-coloured to brownish subcutaneous nodules and plaques on both extremities, both hands, and the joints of the foot for 3–4 years. He complained of pain, but denied pruritus or any other symptoms. He had had hypertension and had been treated with isosorbide-5-mononitrate 50 mg, daily for 10 years. In addition, he had undergone haemodialysis for end-stage renal disease for 8 years. He also underwent amputation of all of his toes due to thromboangitis obliterans 2 years previously. He had recently been diagnosed with hypothyroidism and took 100 µg per day levothyroxine sodium (Synthroxine®, Darim, Seoul, Korea). On physical examination, multiple, various sized, oval-to-linear, firm, fixed, subcutaneous papules, nodules, and plaques were found (Fig. 1). In addition, his skin showed a sclerotic appearance and his joints were not fully extendable. His red blood cell count was  $2.32 \times 10^9/l$  and white blood cell count was  $2.3 \times 10^6/l$ , with 74.3% neutrophil segments, mild anaemia and neutropaenia. Blood urea nitrogen and uric acid levels were within normal limits (23 mg/dl and 4.2 mg/dl, respectively, upper normal limit 24 and 4.5 mg/dl, respectively). However, creatinine level was markedly elevated (4.6 mg/dl) and levels of iron and total iron-binding capacity were decreased (38 µg/dl and 95 µg/dl, respectively). Other haematological and autoimmune markers, including antinuclear antibody, rheumatic factor, antimicrosomal antibody, and extractable nuclear antigen profiles, were not remarkable. A biopsy specimen showed that fine, needle-shaped,

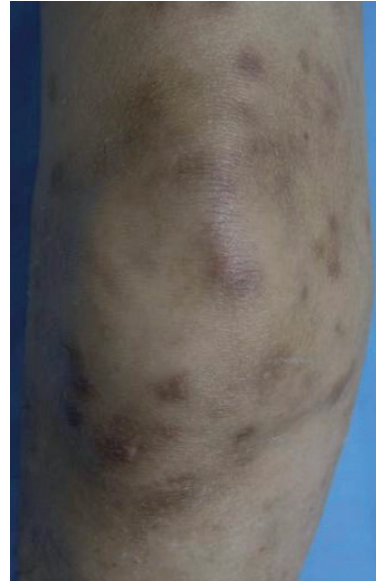


Fig. 1. Multiple, brownish, firm, subcutaneous nodules and plaques on the right knee.

radially arranged crystals surrounded by foreign-body type giant cells and lymphohistiocytes had invaded subcutaneous tissue in alcohol fixation (Fig. 2A). On immunohistochemistry, silver nitrate staining was positive on crystals and Congo red, Alcian blue, von Kossa stain, and Periodic acid-Schiff (PAS) staining were negative (Fig. 2B). Infiltration of numerous crystals and osteosclerosis with scanty haematopoietic cells were observed in the bone marrow (Fig. 2C). Under a polarized microscope with a red filter, the crystals showed characteristic strong negative birefringence. The crystals were yellow when they were parallel to the light, and blue when they were perpendicular to the light according to the rotation of the slow ray axis (Fig. S1; available from <http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1393>). These findings were consistent with gouty panniculitis. On radiological examination, hundreds of soft tissue opacities, which

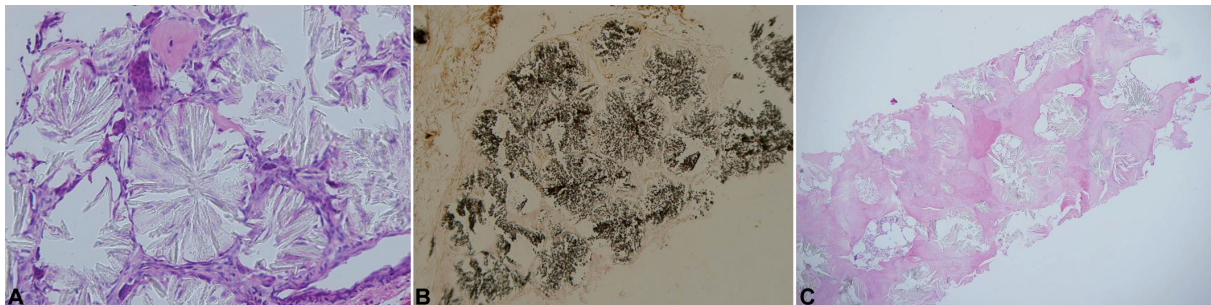


Fig. 2. (A) Fine, needle-shaped, radially-oriented crystals surrounded by foreign-body type giant cells and lymphohistiocytes at the level of the subcutaneous fat layer. (Haematoxylin and eosin (H&E); original magnification,  $\times 200$ ). (B) Crystals stained black in silver nitrate stain on immunohistochemistry (H&E; original magnification,  $\times 100$ ). (C) Infiltration of numerous crystals and osteosclerosis with a scanty haematopoietic cells was observed in bone marrow biopsy specimens (H&E; original magnification,  $\times 40$ ).

varied in size, were observed on both extremities, including the elbow, knee, and hand joints. Computed tomography revealed multiple white opacities on the renal cortex and renal vessels, and severe shrinkage of both kidneys. Combination treatment with allopurinol 200 mg, colchicine 1.2 mg and prednisolone 5 mg per day was initiated, followed by tapering of the dose over the next 2 months. During a follow-up period of approximately one year the patient's renal disease aggravated and his skin lesions were stationary in spite of careful treatments.

## DISCUSSION

Gouty panniculitis was first described in 1977 by Niemi (2), and only 15 cases have been reported since (2–8). The lower extremities are common presenting sites, but it can occur anywhere. Clinical features include solitary or multiple, painful or not, firm nodules or plaques. In the present case urate crystals had deposited not only in subcutaneous tissues of the both extremities, but also in the bone marrow.

The aetiology of gouty panniculitis is not clear; however, it might be related to elevated serum uric acid level as a result of increased synthesis or decreased excretion (5). In addition, antecedent fat damage and circulatory stasis can lead to deposition of urates in the skin (6). In our case, the patient had been treated for end-stage renal failure by haemodialysis. Although his level of uric acid was normal at the time of biopsy, laboratory data, obtained 3 years previously, showed a high value (12.4 mg/dl). Speculatively the uric acid level became normalized in the meantime, but skin lesions did not disappear.

Microscopic examination showed depositions of amorphous eosinophilic material at conventional staining, because formalin fixation washes out the urate crystals. After alcohol fixation, crystals, infiltration of inflammatory cells, and giant cells are found (9). Immunohistochemically, crystals are stained black in silver stain (10) and crystals are doubly refractile in polarized light. The present case presents unique features of fine, radially oriented, needle-shaped crystals with surrounding panniculitis, which showed typical strong negative birefringence under the polariscope.

The differential diagnosis includes a foreign body panniculitis and a calcium deposition diseases. Foreign body panniculitis shows granulomatous inflammation with deposition of hyaluronic acid or amyloid (7). Tumoural calcinosis has deposits of amorphous basophilic materials with surrounding foreign body giant cell reaction, and shows positivity for von Kossa stain and no birefringence (11). Other crystal deposition diseases, such as pseudogout, oxalosis, sclerema neonaturum, post-steroid panniculitis, cold panniculitis, and calciphylaxis, can be

confused with gouty panniculitis (11, 12). In cases of pseudogout, pale, translucent, rhomboid- to rod-shaped crystals with blunt ends are characteristic and crystals show positive birefringence under the polariscope (11). Calcium oxalate crystals of cutaneous oxalosis are yellow to brown and show yellow or blue birefringence, but not negative birefringence, in polarized light (13–15).

Although the optimal treatment for gouty panniculitis has not yet been established, combinations of allopurinol, probenecid, colchicine and anti-inflammatory drugs should be tried to decrease serum uric acid levels, pain and inflammation.

## REFERENCES

1. Underwood M. Diagnosis and management of gout. *BMJ* 2006; 332: 1315–1319.
2. Niemi KM. Panniculitis of the legs with urate crystal deposition. *Arch Dermatol* 1977; 113: 655–656.
3. LeBoit PE, Schneider S. Gout presenting as lobular panniculitis. *Am J Dermatol* 1987; 9: 334–338.
4. Conejo-Mir J, Pulpillo A, Corbi MR, Linares M, Garcia Lopez A, Conde F, et al. Panniculitis and ulcers in a young man. *Arch Dermatol* 1998; 134: 499–504.
5. Snider AA, Barsky S. Gouty panniculitis: a case report and review of the literature. *Cutis* 2005; 76: 54–56.
6. Dahiya A, Leach J, Levy H. Gouty panniculitis in a healthy male. *J Am Acad Dermatol* 2007; 57: S52–S54.
7. Weberschock T, Gholam P, Hartschuh W, Hartmann M. Gouty panniculitis in a 68-year-old man: case report and review of the literature. *Int J Dermatol* 2010; 49: 410–413.
8. Ochoa CD, Valderrama V, Mejia J, Rondon F, Villaroya N, Restrepo JF, et al. Panniculitis: another clinical expression of gout. *Rheumatol Int* 2011; 31: 831–835.
9. Mckee PH, Calonje E, Granter SR. Degenerative and metabolic diseases. In: *Pathology of the skin with clinical correlations*. 3rd edn. Philadelphia: Elsevier Mosby; 2005, p. 590–592.
10. Franke I, Gollnick H. Deposition diseases. In: *Bologna JL, Jorizzo JL, Rapini RP, editors. Dermatology*. 2nd edn. London: Mosby; 2008, p. 633–635.
11. Shidham V, Chivukula M, Basir Z, Shidham G. Evaluation of crystals in formalin-fixed, paraffin-embedded tissue sections for the differential diagnosis of pseudogout, gout, and tumoral calcinosis. *Mod Pathol* 2001; 14: 806–810.
12. Maize JC, Maize JR Jr, Metcalf J. Metabolic diseases of the skin. In: *Elder DE, Elenitsas R, Johnson BL Jr, et al., editors. Lever's histopathology of the skin*. 10th edn. Philadelphia: Lippincott Williams & Wilkins; 2009, p. 438–439.
13. Sina B, Lutz LL. Cutaneous oxalate granuloma. *J Am Acad Dermatol* 1990; 22: 316–318.
14. Isonokami M, Nishida K, Okada N, Yoshikawa K. Cutaneous oxalate granulomas in a haemodialysed patient: report of a case with unique clinical features. *Br J Dermatol* 1993; 128: 690–692.
15. Ohtake N, Uchiyama H, Furue M, Tamaki K. Secondary cutaneous oxalosis: cutaneous deposition of calcium oxalate dihydrate after long-term hemodialysis. *J Am Acad Dermatol* 1994; 31: 368–372.